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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/551,780

11/29/2006

Motoharu Seiki

P28604

5607

7055 7590 12/26/2008
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EXAMINER

HALVORSON, MARK

ART UNIT

PAPER NUMBER

1642

NOTIFICATION DATE

DELIVERY MODE

12/26/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
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Office Action Summary	Application No. 10/551,780	Applicant(s) SEIKI ET AL.	
	Examiner Mark Halvorson	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 9/22/2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 November 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/4/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-33 are pending.

Election/Restrictions

Applicant's election of Group I, claims 1-32, in the reply filed on September 22, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claim 33 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-32 are under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-16, 18, 19, 21-22, 24-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bednarski et al (US Patent Application Publication 20020197210,

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published December 26, 2002, cited previously) in view of Kitagawa et al (J Urol, 1998, 160:1540-1545, Text, 1-8 in cited previously).

The claims are drawn to lipid membrane structure containing an anti-membrane-type matrix metalloproteinase monoclonal antibody, wherein the monoclonal antibody is present in a lipid membrane, on a surface of lipid membrane, in a internal space of lipid membrane, in a lipid layer, and/or on a surface of lipid layer of the lipid membrane structure, wherein the monoclonal antibody binds to a membrane surface of the lipid membrane structure, wherein the monoclonal antibody consists of one or more kinds of monoclonal antibodies selected from an anti-MT1-MMP monoclonal antibody, an anti-MT2-MMP monoclonal antibody, an anti-MT3-MMP monoclonal antibody, an anti-MT4-MMP monoclonal antibody, an anti-MT5-MMP monoclonal antibody, and an anti-MT6-MMP monoclonal antibody, wherein the monoclonal antibody is a human monoclonal antibody or a mouse monoclonal antibody, wherein the monoclonal antibody is a Fab fragment, a F(ab').sub.2 fragment, or a Fab' fragment, wherein the substance for binding the monoclonal antibody to the lipid membrane structure is a lipid derivative that can react with mercapto group in the anti-MT-MMP monoclonal antibody, which contains a phospholipid and/or a phospholipid derivative as a component of the lipid membrane structure, wherein the phospholipid and/or the phospholipid derivative consists of one or more kinds of phospholipids and/or phospholipid derivatives selected from the group consisting of phosphatidylethanolamine, phosphatidylcholine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, cardiolipin, sphingomyelin, ceramide phosphorylethanolamine, ceramide phosphorylglycerol, ceramide phosphorylglycerol phosphate, 1,2-dimyristoyl-1,2-deoxyphosphatidylcholine, plasmalogen and phosphatidic acid, which further contains a sterol as a component of the lipid membrane structure, wherein the sterol is cholesterol and/or cholestanol, which contains a temperature-sensitive lipid derivative as a component in the lipid membrane structure, which contains a pH-sensitive lipid derivative as a component of the lipid membrane structure, which reacts with a membrane-type matrix metalloproteinase on a tumor cell membrane, wherein the tumor cell is an MT-MMP expressing cell, wherein the tumor cell is a cell of fibrosarcoma, squamous carcinoma, neuroblastoma, breast

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carcinoma, gastric cancer, hepatoma, bladder cancer, thyroid tumor, urinary tract epithelial cancer, glioblastoma, acute myeloid leukemia, pancreatic duct cancer or prostate cancer, which reacts with a membrane-type matrix metalloproteinase of a neoplastic vessel, wherein the lipid membrane structure is in the form of micelle, emulsion, liposome or a mixture, which is in a form of dispersion in an aqueous solvent, a lyophilized form, a spray-dried form or a frozen form, a pharmaceutical composition comprising the lipid membrane structure according to claim 1 and a medicinally active ingredient and/or a gene, wherein the medicinally active ingredient and/or gene is present in a lipid membrane, on a surface of lipid membrane, in an internal space of lipid membrane, in a lipid layer and/or on a surface of lipid layer of the lipid membrane structure, wherein the pharmaceutical composition is in a form of a dispersion in an aqueous solvent, a lyophilized form, a spray-dried form, or a frozen form.

Bednarski et al disclose a therapeutic agent comprising a lipid construct, a targeting entity and a therapeutic or treatment entity, (claim 1, paragraph 46) wherein the lipid construct is a liposome, (paragraphs 51-55) the targeting entity is an antibody including monoclonal antibodies and antibody fragments and other antibody-derived molecules which retain specific binding, such as Fab, F(ab')₂, Fv, and scFv derived from antibodies) (paragraph 76-83), which target entities such as the matrix metalloproteases. (claim 15). The therapeutic agent may be used to treat cancer (paragraph 91) The antibody may be attached to the lipid molecules of the liposome through disulfide bonds. (paragraphs 60). The liposome comprise phospholipids, including phosphatidylcholine and phosphatidylethanolamine (paragraph 51), cholesterol (paragraph 53) and stabilizing agents, such as polyethylene glycol, which increase the half-life of the liposome in the circulation. (paragraphs 65-68). The phospholipids of the liposomes are temperature and pH sensitive. Bednarski also discloses therapeutic entities including doxorubicin or other chemotherapeutic agents. (paragraph 48) which may be encapsulated by the liposome or may be associated on the surface of the liposome (paragraph 46). The composition comprising the liposomes can also include other components such as a pharmaceutically acceptable excipients,

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such as water, saline, Ringer's solution, dextrose solution, mannitol, Hank's solution, and other aqueous physiologically balanced salt solutions. (paragraph 88).

Bednarski et al does not disclose a monoclonal antibody consists of one or more kinds of monoclonal antibodies selected from an anti-MT1-MMP monoclonal antibody, an anti-MT2-MMP monoclonal antibody, an anti-MT3-MMP monoclonal antibody, an anti-MT4-MMP monoclonal antibody, an anti-MT5-MMP monoclonal antibody, and an anti-MT6-MMP monoclonal antibody that that targets tumor cells including urinary tract epithelial cancer and reacts with membrane-type matrix metalloproteinase of a neoplastic vessel, wherein the tumor cell is a cell of fibrosarcoma, squamous carcinoma, neuroblastoma, breast carcinoma, gastric cancer, hepatoma, bladder cancer, thyroid tumor, urinary tract epithelial cancer, glioblastoma, acute myeloid leukemia, pancreatic duct cancer or prostate cancer, which reacts with a membrane-type matrix metalloproteinase of a neoplastic vessel

Kitagawa et al discloses an anti-MT1-MMP monoclonal antibody which bound MT1-MMP on tissue specimens of urothelial carcinoma cells. (page 4, 1st paragraph; pae 5 2nd paragraph, Figure 5). The tissue specimens would include neoplastic vessels.

One of ordinary skill in the art would apply Kitagawa et al's monoclonal antibody to MT1-MMP to Bednarski et al's therapeutic agent comprising an immunoliposome because Bednarski et al claims target entities such as the matrix metalloproteases which include the specie MT1-MMP. Furthermore Kitagawa et al disclose that MT1-MMP is expressed on carcinoma cells which would make MT1-MMP a suitable target for Bednarski et als' immunoliposome. It would have been prima facie obvious to combine Bednarski et al's therapeutic agent comprising an immunoliposome with Kitagawa et al's monoclonal antibody to MT1-MMP to make an immunoliposome that recognized MT1-MMP to target urothelial carcinoma cells expressing MT1-MMP.

Claims, 1 and 18-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bednarski et al (cited previously) in view of Kitagawa et al (cited previously) in further view of Cullis et al (US Patent No: 6,417,326, issued July 9, 2002).

The claims are drawn to lipid membrane structure containing an anti-membrane-type matrix metalloproteinase monoclonal antibody, wherein the temperature-sensitive lipid derivative is dipalmitoylphosphatidylcholine, pH-sensitive lipid derivative is dioleoylphosphatidylethanolamine.

Bednarski et al has been described supra.

Bednarski et al does not disclose the phospholipids dipalmitoylphosphatidylcholine and dioleoylphosphatidylethanolamine.

Cullis et al disclose liposomes comprising dipalmitoylphosphatidylcholine (column 10, lines 39-40) and dioleoylphosphatidylethanolamine. (column 14 ,lines 61-65).

One of ordinary skill in the art would have been motivated to apply Cullis et al's disclosure of the phospholipids dipalmitoylphosphatidylcholine and dioleoylphosphatidylethanolamine to Bednarski et al's immunoliposome because Bednarski et al disclosed that the materials which may be utilized in preparing the liposomes include any of the materials known in the art suitable in liposome construction. (paragraph 53). Bednarski et al's also disclosed that such materials include lipids with head groups including phosphatidylcholine and phosphatidylethanolamine. (Id). It would have been prima facie obvious to combine Bednarski et al's immunoliposome with Cullis et al's disclosure of the phospholipids dipalmitoylphosphatidylcholine and dioleoylphosphatidylethanolamine to make an immunoliposome including the phospholipids dipalmitoylphosphatidylcholine and dioleoylphosphatidylethanolamine which are lipids that include the head groups phosphatidylcholine and phosphatidylethanolamine, respectively.

Claims 1 and 14 -17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bednarski et al (, cited previously) in view of Kitagawa et al (cited previously) in further view of Slater et al (US Patent No: 6,355, 268, issued March 12, 2002).

The claims are drawn to lipid membrane structure containing an anti-membrane-type matrix metalloproteinase monoclonal antibody comprising a polyethylene glycol-lipid derivative consisting of one or more kinds of polyethylene glycol-lipid derivatives selected from the group consisting of N-{carbonyl-methoxypolyethylene glycol-2000}-1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine, N-{carbonyl-methoxypolyethylene glycol-5000}-1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine, N-{carbonyl-methoxypolyethylene glycol-750}-1,2-distearoyl-sn-glycero-3-phosphoethanolamine, N-{carbonyl-methoxypolyethylene glycol-2000}-1,2-distearoyl-sn-glycero-3-phosphoethanolamine and N-{carbonyl-methoxypolyethylene glycol-5000}-1,2-distearoyl-sn-glycero-3-phosphoethanolamine.

Bednarski et al has been described supra.

Bednarski et al does not disclose the polyethylene glycol-lipid derivatives selected from the group consisting of N-{carbonyl-methoxypolyethylene glycol-2000}-1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine, N-{carbonyl-methoxypolyethylene glycol-5000}-1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine, N-{carbonyl-methoxypolyethylene glycol-750}-1,2-distearoyl-sn-glycero-3-phosphoethanolamine, N-{carbonyl-methoxypolyethylene glycol-2000}-1,2-distearoyl-sn-glycero-3-phosphoethanolamine and N-{carbonyl-methoxypolyethylene glycol-5000}-1,2-distearoyl-sn-glycero-3-phosphoethanolamine.

Slater et al disclose liposomes comprising N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine. (column 23, lines 14-18).

One of ordinary skill in the art would have been motivated to apply Slater et al's disclosure of the polyethylene glycol-lipid derivative, N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine to Bednarski et al's immunoliposome because Bednarski et al disclosed that the materials which may be utilized in preparing the liposomes include any of the materials known in the art suitable

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in liposome construction and proposes polyethylene glycol as an exemplary stabilizing polymer (paragraph 68). It would have been prima facie obvious to combine Bednarski et al's immunoliposome with Slater et al's disclosure of the polyethylene glycol-lipid derivative, N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine to make an immunoliposome including the stabilizing agent N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine.

Summary

Claims 1-32 stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Mark Halvorson/
Examiner, Art Unit 1642

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